CASWELL FILE

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

FEB 11 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Tribufos (DEF®) Reproduction Studies

TO: Bruce Sidwell PM-53
Reregistration Branch
Special Review and Reregistration Division (H7508C)

FROM: Robert P. Zendzian Ph.D. 1/16/92
Senior Pharmacologist
SACB, HED (H7509C)

THROUGH: Albin Kocialski Ph.D. ABK
Head
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William Burnam
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HED (H7509C)

Compound; Tribufos (DEF®) Tox Chem #864

Registration #074801 Registrant; Mbay

MRID #420402-01, 02 & 03 Tox Project #2-0264

Action Requested

Review the following studies;

Citation

A two-generation dietary reproduction study in rats using Tribufos (DEF®), D.A. Eigenberg; Mobay, Corporate Toxicology Department, Study Number 88-671-AK; Sept 10, 1991; MRID 420401-01

Core Classification Guideline

Conclusion
Doses tested 0. 4. 32 and 260 ppm. Only compound-related effect on reproduction, significant increase in dead pups F1a and F2a litters LEL 260 ppm, NOEL 32 ppm. Most sensitive effect, blood cholinesterase inhibition in adults. LEL for plasma and erythrocyte cholinesterase depression 4 ppm (LDT),

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No NOEL. In pups, decreased cholinesterase activity greatest 21 days in the F1a females plasma cholinesterase activity significantly decreased LEL 32 ppm, NOEL 4 ppm.

Citation

A Cross-Fostering study in rats using Tribufos (DEF®) administered in the diet, D.A. Eigenberg; Mobay, Corporate Toxicology Department, Study Number 88-971-BZ; Aug 29, 1991; MRID 420401-03

Core Classification Acceptable

Conclusion

Cross fostering study to determine if pup loss in study 88-671-AK was due to treatment of dams, pups in utero or both. Doses tested 0 and 260 ppm. Group II negative control-untreated pups & dams, Group I experimental-treated pups untreated dams, Group III experimental-untreated pups treated dams, Group IV positive control-treated pups treated dams. Mean pup loss 0.00, 0.47, 1.50 & 2.85 respectively. Cannibalism in treated dam groups (III & IV). Evidence for both mechanisms plus a synergistic effect in group IV.

Citation

A dietary reproductive toxicity study investigation the fertility of F1 rats using Tribufos (DEF®), D.A. Eigenberg; Mobay, Corporate Toxicology Department, Study Number 88-971-DC; Aug 27, 1991; MRID 420401-02

Core Classification Unacceptable

Conclusion

The following footnotes were contained in the report;
"Due to an error, the control and 260 ppm rats received a mixture of control and 260 ppm feed for one day during week 13 of the study (i.e., mating/gestation phase).
"Due to a feeding error, terminal cholinesterase values were obtained from 6 high dose and 8 control animals."
No explanation was found in the test. It is not certain how the feeding errors, particularly the second might have affected the study. This may have been of critical importance since only 8 control and 6 high dose females were available for cholinesterase analysis out of 30 females on each dose.

Attachments
DERs
1-liners

Data Evaluation Report 009140

Compound Tribufos (DEF)

Citation
A two-generation dietary reproduction study in rats using Tribufos (DEF®), D.A. Eigenberg; Mobay, Corporate Toxicology Department, Study Number 88-671-AK; Sept 10, 1991; MRID 420401-01

1/13/92

Reviewed by Robert P. Zendzian Ph.D.
Senior Pharmacologist
Health Effects Division

Core Classification Guideline

Conclusion
Doses tested 0. 4. 32 and 260 ppm. Only compound-related effect on reproduction, significant increase in dead pups F1a and F2a litters LEL 260 ppm, NOEL 32 ppm. Most sensitive effect blood cholinesterase inhibition in adults. LEL for plasma and erythrocyte cholinesterase depression 4 ppm (LDT), No NOEL. In pups, decreased cholinesterase activity greatest 21 days in the F1a females plasma cholinesterase activity significantly decreased LEL 32 ppm, NOEL 4 ppm.

Materials

Technical grade Tribufos
Straw colored liquid
Batch No; 85R-26-39
98.5% (3/88)
99.7% (9/88)
98.8% (3/89)
From Mobay Ag Chemicals Division

Male and female albino CD Sprague-Dawley rats, six-eight weeks old,
from Sasco Inc Omaha Nebraska

Experimental Design

Thirty males and thirty females were assigned randomly to each of four test groups and dosed with 0, 4, 32 and 260 ppm tribufos in the diet. After 10 weeks on the test diet these F0 animals were bred within their test groups. Thirty males and thirty females were selected from the weanlings of each test group to parent the second generation. After 10 weeks on the test diet these F1 animals were bred within their test groups.

Test material analysis

Test material was analyzed for identity, recovery in the feed, homogeneity in the feed, stability in the feed and concentration in the feed.

Breeding

One male and one female were cohabited for breeding for up to 21 days. Females were checked daily for vaginal plug and vaginal smears examined for sperm. When sperm was observed females were housed individually for gestation and lactation. Unmated females were cohabited with a second proven male for up to 7 days. Whether or not breeding was observed these females were subsiquently housed individually for gestation and lactation.

Estrous cycle staging

"Vaginal smears were taken for two weeks from ten F0 and F1 females/dose and classified as diestrous, proestrous proestrous/esterus or estrous."

Clinical observations

Rats were observed daily for morbidity, mortality and clinical signs in the cage. Animals were individually examined weekly. Body weight and food consumption were measured weekly for each male and female. During gestation female body weight was determined on days 0, 6, 13 and 20 of gestation and days 1, 4, 7, 14 and 21 of lactation and food consumption weekly during gestation, twice during week one of lactation and once weekly during weeks 2 and 3

Live and still born pups and sex distribution were determined for each litter. Litter counts were performed daily and pup weights obtained within 24 hours of birth (day 0) and on days 4, 7, 14 and 21. Each litter was culled on day 4 to 8 pups, 4 males and 4 females were possible. Culls were sacrificed and subject to gross necropsy.

Plasma, red blood cell and brain cholinesterase were determined on 10 F0 and F1 adults, plasma and RBC during week 8 and just prior to sacrifice and brain at termination. Plasma, RBC and brain cholinesterase were determined for one male and one female pup each from ten litters at culling (day 4 post partum) and at weaning (day 21 post partum).

Sacrifice/Necropsy/Histology

Culled pups were sacrificed by injection of euthanasia solution, adults and weanlings by CO_2 asphyxiation. All animals were subject to gross necropsy.

"F0 and F1 adult males were sacrificed after the last F1a and F2a litters, respectively, were delivered and/or the dams had gone past day 24 of gestation. A complete gross necropsy was performed and testicle and terminal body weights were measured. The testes, pituitary, epididymides, seminal

vesicles/coagulating gland, prostrate gland and gross lesions were collected and fixed in Bouin's fixative."

"F0 and F1 adult females were sacrificed after each dam's pups were weaned/died or when day 24 of gestation was reached. Ovary and terminal body weights were measured. The pituitary, vagina, cervix, uterus, ovaries and gross lesions were collected and fixed in Bouin's fixative. The uterus from all dams was examined for implantation sites, and the number of sites were counted."

Results

Analysis of dosed feed showed that test material was homeogeniously distributed and stable for 14 days at room temperature.

No clinical signs indicative of cholinesterase toxicity were observed.

Weight and feed consumption of females during gestation and lactation is presented in Table from the report. At the high dose (260ppm) F0 dams were reduced in weigh at gestation day 20 and throughout the lactation period and feed consumption was reduced throughout lactation. At the high dose (260ppm) F1 dams were reduced in weigh throughout the lactation period and feed consumption was reduced on days 14 and 21 of lactation.

No compound-related effect on mortality was observed in the adult rats. A statistically significant increase in pup mortality was observed at the high dose in both generations. Pups found dead, due to cannibalism or other causes, were as follows;

Dose	F1a	F2a
ppm	dead/total	dead/total
0	11/317	6/333
4	18/339	7/307
32	5/320	5/320
260	93/289	57/253

Mating and fertility induces are presented in Table 6 from the report. The fertility index of the F1 dams was depressed at 260 ppm.

Insemination and gestation lengths are summarized in Table 7 from the report. Gestation length was significantly increased at 260 ppm for the F2a litters.

Implantation sites and gestation, birth and live birth indices for the F0 and F1 dams are sumarized in Table 8 from the report. Birth index and live birth index were significanlty reduced for both generations at 260 ppm.

Gender mean data for pups are summarized in Table 9 from the report. In the F1a litters the portion of male pups is

decreased and the number of unknown sex pups is increased significantly. In the F2a litters the number of unknown sex pups is increased significantly.

Litter viability is summarized in Table 10 from the report. For the F0 dams - F1a pups litter size was significantly reduced at birth and the viability index significantly reduced at days 4, 14 and 21 at 260 ppm. For the F1 dams - F2a pups litter the viability index was significantly reduced at days 4 and 21 at 260 ppm.

Number of litters with stillborn pups is summarized in Table 11 from the report. The number of litters with stillbirths is significantly increased for the F1 and F2 mating at 260 ppm.

Pup weight weight data are summarized in Table 13 from the Report. F1a pup mean weight is significantly decreased at 260 ppm on days 0, 4, 7, 14 and 21. F2a pup mean weight is significantly decreased on days 7, 14 and 21.

Pup cholinesterase activity is summarized in Table CC1-SUM from the report. In the F1a litters erythrocyte and brain cholinesterase activity were significantly decreased at 260 ppm in the females at day 4. In the same litters at day 21, a strange observation was the significant increase in brain cholinesterase activity at 4 ppm in both sexes. In the males plasma cholinesterase activity was significantly decreased at 260 ppm. In the females plasma cholinesterase activity was significantly decreased at 32 and 260 ppm and erythrocyte activity at 260 ppm.

In the F2a litters no significant effects were observed at 4 days. At 21 days plasma, erythrocyte and brain cholinesterase activity were significantly decreased in both sexes at 260 ppm.

Adult cholinesterase activity is summarized in Table CC3-SUM from the report. In the F0 males plasma and erythrocyte cholinesterase activity were significantly decreased at 32 and 260 ppm for both samples and in the brain at 260 ppm. In the F0 females plasma and erythrocyte cholinesterase activity were significantly decreased at 4 ppm at day 114 but not at day 56. Plasma, erythrocyte and brain cholinesterase activity were significantly decreased for all samples at 32 and 260 ppm.

In the F1 males erythrocyte cholinesterase activity was significantly decreased at 4 ppm on day 62 and on both days at 32 ppm. Plasma, erythrocyte and brain cholinesterase activity were significantly decreased for all samples at 260 ppm. In the F1 females erythrocyte cholinesterase activity was significantly decreased at 4 ppm at day 90 but not at day 62. Plasma, erythrocyte and brain cholinesterase activity was significantly decreased for all samples at 32 and 260 ppm.

No compound-related histopathological abnormalities were observed.

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Discussion

The only compound-related effect on reproduction was a significant increase in dead pups in both the F1a and F2a litters at 260 ppm (NOEL 32 ppm).

The most sensitive compound-related effect was blood cholinesterase inhibition in the adults. Statistically significant effects are summarized in Table CC4-SUM from the report. The LEL for plasma and erythrocyte cholinesterase depression was 4 ppm (LDT). A NOEL was not determined.

In the pups, decreased cholinesterase activity was greatest at 21 days in the F1a females where plasma cholinesterase activity was significantly decreased at 32 ppm (NOEL 4 ppm).

MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT REPRODUCTION STUDY WITH DEF
STUDY NUMBER 88-671-AK
FO DAMS - F1A MATINGS GESTATION AND LACTATION

TABLE: 5 BODY WEIGHT (G) MEAN & STANDARD DEVIATION

LEVEL	GW0	GW6	GW13	GW20	GWCHG	LW1	LW4	LW7	LW14	LW21	LWCHG
CONTROL	256	271	298	376	121	286	301	306	333	315	29
	24	23	25	31	15	25	27	26	25	21	19
4 PPM	259	278	302	379	120	294	308	315	332	326	32
	23	23	24	36	19	26	21	22	30	22	15
32 PPM	257	273	299	378	122	293	313	317	332	322	29
	21	23	25	32	19	26	28	30	35	27	13
260 PPM	248	262	284	348*	100*	269	278 *	282 *	294 *	283*	19 *
	24	29	30	38	14	29	32	31	33	33	21

FEED CONSUMPTION (G) MEAN & STANDARD DEVIATION

LEVEL	GFC6	GFC13	GFC20	LFC4	LFC7	LFC14	LFC21
CONTROL	106	136	152	103	124	366	448
	18	17	13	33	26	36	56
4 PPM	105	139	158	94	122	350	467
	11	10	15	15	16	49	61
32 PPM	101	141	159	98	128	371	465
	17	34	15	12	23	44	48
260 PPM	104	138	150	77 *	101 *	285 *	328 *
	13	13	14	24	28	45	59

* = Statistically significantly different from the Control group ($p \leq 0.05$).

MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT REPRODUCTION STUDY WITH DEF
STUDY NUMBER 88-871-AK
F1 DAMS - F2A MATINGS GESTATION AND LACTATION

TABLE: 5 BODY WEIGHT (G) MEAN & STANDARD DEVIATION

LEVEL	GW0	GW6	GW13	GW20	GWCHG	LW1	LW4	LW7	LW14	LW21	LWCHG
CONTROL	253	269	290	358	105	279	291	297	307	308	29
	23	26	25	34	26	25	27	29	30	28	21
4 PPM	255	276	299	374	119	290	302	300	319	308	18
	20	20	23	30	28	23	24	22	23	29	20
32 PPM	259	279	303	386 *	127 *	294	311 *	308	322	320	28
	24	23	25	32	15	23	27	23	27	25	14
280 PPM	237	252	274	338	101	259 *	268 *	268 *	280 *	277 *	18
	35	37	42	54	24	33	37	41	40	33	9

FEED CONSUMPTION (G) MEAN & STANDARD DEVIATION

LEVEL	GFC6	GFC13	GFC20	LFC4	LFC7	LFC14	LFC21
CONTROL	96	137	155	94	118	358	469
	18	12	31	21	15	44	58
4 PPM	104	145	184	101	123	358	481
	11	11	12	22	10	33	37
32 PPM	105	147	168	111	132 *	378	496
	11	16	14	27	16	45	45
280 PPM	102	143	155	94	115	312 *	372 *
	13	22	22	26	38	90	85

* = Statistically dignificantly different from the Control group ($p \leq 0.05$).

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TABLE 6

Mating and Fertility Indices of F1 Dams in a Rat Reproduction Study Using Technical Tribufos

Study Number 88-671-AK

Dose Group	Number Co-housed	Number Sperm Positive	Number Delivered	Number with Implantation Sites	Mating Index	Fertility Index
Control	30	30	29	29	100	97
4.0 ppm	29	29	27	27	100	93
32.0 ppm	30	29	25	26	97	90
260.0 ppm	29	29	22	22	100	76

$$\text{Mating Index (\%)} = \frac{\text{\# of sperm positive females}}{\text{\# of females co-housed with males}} \times 100$$

$$\text{Fertility Index (\%)} = \frac{\text{\# of pregnant females (a)}}{\text{\# of sperm positive females}} \times 100$$

(a) Females that deliver and/or have implantation sites.

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TABLE 6

Mating and Fertility Indices of F0 Dams in a Rat Reproduction Study Using Technical Tribufos

Study Number 88-671-AK

Dose Group	Number Co-housed	Number Sperm Positive	Number Delivered	Number with Implantation Sites	Mating Index	Fertility Index
Control	29	29	26	26	100	90
4.0 ppm	30	30	29	29	100	97
32.0 ppm	30	30	27	27	100	90
260.0 ppm	30	29	26	25	97	90

$$\text{Mating Index (\%)} = \frac{\text{\# of sperm positive females}}{\text{\# of females co-housed with males}} \times 100$$

$$\text{Fertility Index (\%)} = \frac{\text{\# of pregnant females (a)}}{\text{\# of sperm positive females}} \times 100$$

(a) Females that deliver and/or have implantation sites.

TABLE 7

Insemination and Gestation Lengths in a Rat Reproduction Study Using Technical Tribufos (mean and standard deviation)

Study Number 88-671-AK

	INSEMINATION LENGTHS (DAYS)		GESTATION LENGTHS (DAYS)	
	F1a	F2a	F1a	F2a
CONTROL	2.5 1.2	3.8 3.9	21.8 0.5	21.8 0.5
4.0 ppm	2.5 1.1	2.6 2.5	22.0 0.7	22.0 0.5
32.0 ppm	2.7 1.5	3.0 3.0	21.9 0.6	22.0 0.4
260.0 ppm	3.6 3.6	3.5 3.1	22.2 0.7	22.4 * 0.7

* = Statistically significantly different from the Control group ($p \leq 0.05$).

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TABLE 8

Implantation Sites, and Gestation, Birth and Live Birth Indices for F0 anf F1 Dams in a Rat Reproduction Study Using Technical Tribufos (mean and standard deviation)

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Study Number 88-671-AK

	GESTATION INDEX (%)		IMPLANTATION SITES	
	F1a	F2a	F1a	F2a
CONTROL	100	100	13	12
			2	3
4 ppm	100	96	13	12
			2	3
32 ppm	100	96	13	14 *
			2	3
260 ppm	92	95	13	11
			2	4

	BIRTH INDEX (%)		LIVE BIRTH INDEX (%)	
	F1a	F2a	F1a	F2a
CONTROL	91	92	100	99
	7	11	1	4
4 ppm	89	91	97	99
	11	14	11	3
32 ppm	90	92	100	100
	13	7	0	2
260 ppm	77 *	87	87 *	91 *
	16	17	21	14

* = Statistically significantly different from the control group ($p \leq 0.05$) with a Bonnferroni adjustment where applicable.

Gestation index (%) = $\frac{\text{\# of females with live pups}}{\text{\# of pregnant females}} \times 100$

Birth index (%) = $\frac{\text{Total \# of pups born/litter}}{\text{Total \# of implantation sites/litter}} \times 100$

Live Birth index (%) = $\frac{\text{Live pups born/litter}}{\text{Total \# of pups/litter}} \times 100$

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MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT REPRODUCTION STUDY WITH DEF
STUDY NUMBER 88-871-AK
F1A - PUP GENDER

TABLE: 9 GENDER MEAN & STANDARD DEVIATION

LEVEL	MALE PUP	FEMALE PUP	UNKNOWN PUP
CONTROL	8	7	0
	2	2	0
4 PPM	8	8	0
	2	2	0
32 PPM	8	8	0
	2	2	0
260 PPM	3	8	1
	2	3	1

MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT REPRODUCTION STUDY WITH DEF
STUDY NUMBER 88-871-AK
F2A - PUP GENDER

GENDER MEAN & STANDARD DEVIATION

LEVEL	MALE PUP	FEMALE PUP	UNKNOWN PUP
CONTROL	8	8	0
	2	2	0
4 PPM	5	6	0
	2	2	0
32 PPM	8	7	0
	2	2	0
260 PPM	5	5	0
	3	2	1

GENDER PERCENT MEAN & STANDARD DEVIATION

LEVEL	MALE PUP	FEMALE PUP	UNKNOWN PUP
CONTROL	47	53	0
	11	11	0
4 PPM	51	48	2
	14	14	6
32 PPM	52	48	0
	13	13	0
260 PPM	38 *	53	9 *
	15	19	15

GENDER PERCENT MEAN & STANDARD DEVIATION

LEVEL	MALE PUP	FEMALE PUP	UNKNOWN PUP
CONTROL	48	52	0
	14	14	0
4 PPM	47	52	1
	18	18	4
32 PPM	47	53	0
	14	14	0
260 PPM	48	48	5 *
	18	17	8

* = Statistically significantly different from the Control group ($p \leq 0.05$).

MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT REPRODUCTION STUDY WITH DEF
STUDY NUMBER 88-871-AK : FO DAMS - F1A PUPS
LITTER COUNTS

TABLE: 10 LITTER VIABILITY MEAN & STANDARD DEVIATION

LEVEL	LITTER SIZE	STILL BORN	UNKNOWN	LIVE COUNT DAY 0	LIVE COUNT DAY4 PRECULL	LIVE COUNT DAY4 POSTCULL	LIVE COUNT DAY 7	LIVE COUNT DAY 14	LIVE COUNT DAY 21
CONTROL	12	0	0	12	12	8	8	8	8
	2	0	0	2	3	1	1	1	1
4 PPM	12	0	0	12	11	7	7	7	7
	2	0	1	3	3	2	2	2	2
32 PPM	12	0	0	12	12	8	8	8	8
	2	0	0	2	2	0	0	0	0
280 PPM	10 *	1	1*	8	6	5	5	4	4
	3	1	2	4	5	3	4	4	4

LEVEL	VIABILITY INDEX DAY 4	VIABILITY INDEX DAY 7	VIABILITY INDEX DAY 14	VIABILITY INDEX DAY 21
CONTROL	96	100	100	100
	13	0	0	0
4 PPM	96	98	98	98
	18	5	5	5
32 PPM	100	100	99	99
	1	2	3	4
280 PPM	73*	94	83 *	83*
	40	23	37	37

* = Statistically significantly different from the Control group ($p \leq 0.05$).

MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT REPRODUCTION STUDY WITH DEF
STUDY NUMBER 88-671-AK : F1 DAMS - F2A PUPS
LITTER COUNTS

TABLE: 10 LITTER VIABILITY MEAN & STANDARD DEVIATION

LEVEL	LITTER SIZE	STILL BORN	UNKNOWN	LIVE COUNT DAY 0	LIVE COUNT DAY4 PRECULL	LIVE COUNT DAY4 POSTCULL	LIVE COUNT DAY 7	LIVE COUNT DAY 14	LIVE COUNT DAY 21
CONTROL	11	0	0	11	11	8	8	8	8
	3	1	0	3	3	1	1	1	1
4 PPM	11	0	0	11	11	8	8	8	7
	3	0	0	3	3	2	2	2	2
32 PPM	12	0	0	12	12	7	7	7	7
	4	0	0	4	4	2	2	2	2
260 PPM	10	1	0*	9	7	6	6	6	5
	3	3	1	4	5	3	3	3	3

LEVEL	VIABILITY INDEX DAY 4	VIABILITY INDEX DAY 7	VIABILITY INDEX DAY 14	VIABILITY INDEX DAY 21
CONTROL	97	100	100	100
	10	2	2	2
4 PPM	100	100	100	99
	2	0	2	3
32 PPM	97	99	99	99
	8	3	3	3
260 PPM	81 *	95	91	80*
	33	23	25	25

* = Statistically significantly different from the Control group ($p \leq 0.05$).

TABLE 11

Litters With Stillborn Pups in a Rat Reproduction Study Using Technical Tribufos

Study Number 88-671-AK

MATING	LEVEL	# OF LITTERS WITH STILLBIRTHS	# OF LITTERS DELIVERED
F1	0 ppm	1	26
	4.0 ppm	0	29
	32.0 ppm	0	27
	260.0 ppm	6 *	25
F2	0 ppm	2	29
	4.0 ppm	3	27
	32.0 ppm	1	25
	260.0 ppm	8 *	22

* = Statistically significantly different from the Control group ($p \leq 0.05$).

MOBAY CORPORATION
CORPORATE TOXICOLOGY DEPARTMENT
RAT REPRODUCTION STUDY WITH DEF

STUDY NUMBER 88-671-AK
F1A - AVERAGE PUP WEIGHTS

TABLE: 13 WEIGHT (G) MEAN & STANDARD DEVIATION

LEVEL	WTDAY0	WTDAY4	WTDAY7	WTDAY14	WTDAY21
CONTROL	7.1 0.6	10.0 1.2	16.0 1.8	31.5 2.5	49.5 5.5
4 PPM	7.1 0.7	9.8 1.5	15.6 2.3	30.5 3.4	50.2 6.0
32 PPM	7.2 0.8	10.1 1.2	16.1 1.7	31.1 3.3	50.1 5.8
280 PPM	6.3* 0.6	7.8* 1.8	11.2* 3.0	23.1* 3.7	35.2* 6.2

MOBAY CORPORATION
CORPORATE TOXICOLOGY DEPARTMENT
RAT REPRODUCTION STUDY WITH DEF

STUDY NUMBER 88-671-AK
F2A - AVERAGE PUP WEIGHTS

TABLE: 13 WEIGHT (G) MEAN & STANDARD DEVIATION

LEVEL	WTDAY0	WTDAY4	WTDAY7	WTDAY14	WTDAY21
CONTROL	6.8 0.8	9.6 1.5	15.2 2.0	30.5 4.6	49.1 5.8
4 PPM	7.2* 0.5	10.2 1.0	16.4* 1.5	30.8 2.4	49.5 4.8
32 PPM	7.0 0.5	9.9 1.4	16.2 1.7	30.5 2.6	50.2 5.8
280 PPM	6.7 0.8	8.7 1.5	13.0* 2.0	23.9* 3.6	38.3* 5.9

* = Statistically significantly different from the Control group ($p \leq 0.05$).

MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT

TABLE CC1-SUM

COMPOUND: TRIBUFOS
STUDY #: 88-671-AK
STUDY TYPE: REPRODUCTION

PUP CHOLINESTERASE SUMMARY (PLASMA, ERYTHROCYTE AND BRAIN VALUES)

SEX: BOTH
SPECIES: RAT
DURATION: TWO-GENERATION

LITTER F1A,
PUP AGE 4-DAY,
AND PUP SEX M

		DOSAGE GROUP			
		CONTROL	4 PPM	32 PPM	280 PPM
PLASMA CHOLINESTERASE	MEAN	0.59	0.57	0.61	0.53
	STD	0.09	0.08	0.07	0.03
	N	10.00	10.00	10.00	2.00
ERYTHROCYTE CHOLINESTERASE	MEAN	2.95	* 2.69	2.86	2.93
	STD	0.11	0.22	0.21	0.40
	N	10.00	10.00	10.00	2.00
BRAIN CHOLINESTERASE	MEAN	4.44	4.32	4.32	4.06
	STD	0.50	0.36	0.36	0.11
	N	10.00	10.00	10.00	2.00

LITTER F1A,
PUP AGE 4-DAY,
AND PUP SEX F

		DOSAGE GROUP			
		CONTROL	4 PPM	32 PPM	280 PPM
PLASMA CHOLINESTERASE	MEAN	0.61	0.61	0.59	0.58
	STD	0.08	0.11	0.08	0.09
	N	10.00	10.00	10.00	10.00
ERYTHROCYTE CHOLINESTERASE	MEAN	2.86	2.62	2.79	* 2.47
	STD	0.32	0.44	0.21	0.37
	N	10.00	10.00	10.00	10.00
BRAIN CHOLINESTERASE	MEAN	4.56	4.43	4.42	* 4.00
	STD	0.50	0.54	0.30	0.41
	N	10.00	10.00	10.00	10.00

* = SIGNIFICANTLY DIFFERENT FROM CONTROL VALUE (P<=0.05).

TABLE CC1-SUM

COMPOUND: TRIBUFOS
STUDY #: 88-871-AK
STUDY TYPE: REPRODUCTION

PUP CHOLINESTERASE SUMMARY (PLASMA, ERYTHROCYTE AND BRAIN VALUES)

SEX: BOTH
SPECIES: RAT
DURATION: TWO-GENERATION

LITTER F1A,
PUP AGE 21-DAY,
AND PUP SEX M

		DOSAGE GROUP			
		CONTROL	4 PPM	32 PPM	280 PPM
PLASMA CHOLINESTERASE	MEAN	0.69	0.67	0.57	* 0.44
	STD	0.15	0.12	0.10	0.18
	N	10.00	10.00	10.00	10.00
ERYTHROCYTE CHOLINESTERASE	MEAN	3.01	* 3.39	3.20	2.67
	STD	0.24	0.34	0.43	0.68
	N	10.00	10.00	10.00	10.00
BRAIN CHOLINESTERASE	MEAN	11.82	* 14.18	13.07	10.84
	STD	0.37	0.82	1.35	1.24
	N	10.00	10.00	10.00	10.00

LITTER F1A,
PUP AGE 21-DAY,
AND PUP SEX F

		DOSAGE GROUP			
		CONTROL	4 PPM	32 PPM	280 PPM
PLASMA CHOLINESTERASE	MEAN	0.65	0.72	* 0.53	* 0.40
	STD	0.10	0.11	0.08	0.14
	N	10.00	10.00	10.00	7.00
ERYTHROCYTE CHOLINESTERASE	MEAN	3.33	3.40	3.20	* 2.58
	STD	0.30	0.24	0.31	0.59
	N	10.00	10.00	10.00	7.00
BRAIN CHOLINESTERASE	MEAN	12.07	* 14.33	12.44	11.30
	STD	0.68	1.48	0.91	1.78
	N	10.00	10.00	10.00	7.00

* = SIGNIFICANTLY DIFFERENT FROM CONTROL VALUE (P<=0.05).

COMPOUND: TRIBUFOS
STUDY #: 88-671-AK
STUDY TYPE: REPRODUCTION

TABLE CC1:SUM

PUP CHOLINESTERASE SUMMARY (PLASMA, ERYTHROCYTE AND BRAIN VALUES)

SEX: BOTH
SPECIES: RAT
DURATION: TWO-GENERATION

LITTER F2A,
PUP AGE 4-DAY,
AND PUP SEX M

		DOSAGE GROUP			
		CONTROL	4 PPM	32 PPM	280 PPM
PLASMA CHOLINESTERASE	MEAN	0.59	0.62	0.64	0.62
	STD	0.07	0.09	0.10	0.06
	N	10.00	10.00	10.00	9.00
ERYTHROCYTE CHOLINESTERASE	MEAN	3.34	3.49	3.32	3.07
	STD	0.34	0.25	0.20	0.20
	N	10.00	10.00	10.00	9.00
BRAIN CHOLINESTERASE	MEAN	4.47	4.61	4.49	4.39
	STD	0.25	0.33	0.26	0.37
	N	10.00	10.00	10.00	9.00

LITTER F2A,
PUP AGE 4-DAY,
AND PUP SEX F

		DOSAGE GROUP			
		CONTROL	4 PPM	32 PPM	280 PPM
PLASMA CHOLINESTERASE	MEAN	0.62	0.65	0.59	0.63
	STD	0.06	0.08	0.10	0.09
	N	10.00	10.00	10.00	8.00
ERYTHROCYTE CHOLINESTERASE	MEAN	3.34	3.37	3.21	3.11
	STD	0.35	0.44	0.19	0.37
	N	10.00	10.00	10.00	8.00
BRAIN CHOLINESTERASE	MEAN	4.60	4.56	4.54	4.45
	STD	0.27	0.18	0.29	0.39
	N	10.00	10.00	10.00	8.00

* = SIGNIFICANTLY DIFFERENT FROM CONTROL VALUE (P<=0.05).

MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT

TABLE CC1-SUM

COMPOUND: TRIBUFOS
STUDY #: 88-671-AK
STUDY TYPE: REPRODUCTION

PUP CHOLINESTERASE SUMMARY (PLASMA, ERYTHROCYTE AND BRAIN VALUES)

SEX: BOTH
SPECIES: RAT
DURATION: TWO-GENERATION

LITTER F2A,
PUP AGE 21-DAY,
AND PUP SEX M

		DOSAGE GROUP			
		CONTROL	4 PPM	32 PPM	280 PPM
PLASMA CHOLINESTERASE	MEAN	0.61	0.66	0.48	*0.30
	STD	0.10	0.12	0.08	0.16
	N	10.00	11.00	10.00	10.00
ERYTHROCYTE CHOLINESTERASE	MEAN	2.75	2.95	2.74	*2.08
	STD	0.20	0.35	0.33	0.82
	N	10.00	11.00	10.00	10.00
BRAIN CHOLINESTERASE	MEAN	11.53	11.68	11.38	*9.85
	STD	0.36	0.46	0.51	1.40
	N	10.00	10.00	10.00	10.00

LITTER F2A,
PUP AGE 21-DAY,
AND PUP SEX F

		DOSAGE GROUP			
		CONTROL	4 PPM	32 PPM	280 PPM
PLASMA CHOLINESTERASE	MEAN	0.58	0.69	0.52	*0.21
	STD	0.13	0.11	0.14	0.11
	N	10.00	10.00	10.00	10.00
ERYTHROCYTE CHOLINESTERASE	MEAN	2.78	2.98	2.80	*1.70
	STD	0.27	0.30	0.39	0.45
	N	10.00	10.00	10.00	10.00
BRAIN CHOLINESTERASE	MEAN	11.64	11.66	11.66	*9.85
	STD	0.38	0.86	0.25	0.97
	N	10.00	9.00	10.00	10.00

* = SIGNIFICANTLY DIFFERENT FROM CONTROL VALUE (P<=0.05).

MOBAY Toxicology Department
Study : 88-671-AK-F1
Species : Rat
Generation : F0

A TWO-GENERATION REPRODUCTION
STUDY IN RATS WITH DEF
STUDY NUMBER 88-671-AK(F0)

Date : 21-JAN-91
Time : 15:13:19
Page : 1

MEAN Serum Chemistry — Brain Cholinesterase — Nominal days in study @ 127

MALES		Day 56 PCho IU/ml	Day 56 RCho IU/ml	Day 127 PCho IU/ml	Day 127 RCho IU/ml	MALES		
0 PPM	Mean	0.56	2.63	0.50	2.85	0 PPM	Mean	12.4
	SD	0.11	0.16	0.10	0.16		SD	0.5
	n	10	10	10	10		n	10
4 PPM	Mean	0.54	2.66	0.49	2.83	4 PPM	Mean	12.5
	SD	0.12	0.16	0.09	0.17		SD	0.9
	n	10	10	10	10		n	10
32 PPM	Mean	0.38*	1.72*	0.41*	1.96*	32 PPM	Mean	12.7
	SD	0.12	0.20	0.06	0.09		SD	0.7
	n	10	10	10	10		n	10
260 PPM	Mean	0.17*	1.31*	0.11*	1.35*	260 PPM	Mean	7.9*
	SD	0.06	0.18	0.03	0.04		SD	0.8
	n	10	10	10	10		n	10

FEMALES		Day 56 PCho IU/ml	Day 56 RCho IU/ml	Day 114 PCho IU/ml	Day 114 RCho IU/ml	FEMALES		
							Day 114	
0 PPM	Mean	1.00	2.51	0.94	2.88	0 PPM	Mean	12.8
	SD	0.62	0.14	0.17	0.14		SD	1.1
	n	10	10	10	10		n	10
4 PPM	Mean	1.57	2.56	0.70*	2.52*	4 PPM	Mean	12.5
	SD	0.57	0.14	0.16	0.20		SD	0.5
	n	10	10	10	10		n	10
32 PPM	Mean	0.58*	1.58*	0.26*	1.56*	32 PPM	Mean	9.1*
	SD	0.19	0.20	0.06	0.09		SD	1.2
	n	10	10	10	10		n	10
260 PPM	Mean	0.16*	1.28*	0.09*	1.38*	260 PPM	Mean	2.4*
	SD	0.09	0.14	0.02	0.09		SD	0.7
	n	10	10	10	10		n	10

Statistics: Anova + Dunnetts tests (two-sided): * P<0.05 (Exp.Unit = Animal)

OC3-SUM

MOBAY Toxicology Department
Study : 88-671-AK-F2
Species : Rat
All subsets

A TWO-GENERATION REPRODUCTION
STUDY IN RATS WITH DEF
STUDY NUMBER 88-671-AK(F1)

Date : 22-JAN-91
Time : 11:21:47
Page : 1

M E A N S e r u m C h e m i s t r y

M A L E S		Day 62 PChe IU/ml	Day 62 RChe IU/ml	Day 111 PChe IU/ml	Day 111 RChe IU/ml	Day 111 BChe IU/g
0 PPM	Mean	0.46	3.36	0.53	3.21	13.4
	SD	0.08	0.21	0.13	0.26	0.4
	n	10	10	10	10	10
4 PPM	Mean	0.49	3.05*	0.59	3.05	13.5
	SD	0.11	0.17	0.21	0.12	0.8
	n	10	10	10	10	10
32 PPM	Mean	0.44	2.48*	0.52	2.32*	13.6
	SD	0.11	0.09	0.17	0.19	0.6
	n	10	10	10	10	10
260 PPM	Mean	0.20*	1.93*	0.17*	1.97*	9.0*
	SD	0.16	0.11	0.11	0.32	1.1
	n	10	10	10	10	10

F E M A L E S		Day 62 PChe IU/ml	Day 62 RChe IU/ml	Day 90 PChe IU/ml	Day 90 RChe IU/ml	Day 90 BChe IU/g
0 PPM	Mean	1.44	3.11	0.83	2.36	13.2
	SD	0.53	0.18	0.22	0.18	0.7
	n	10	10	10	10	10
4 PPM	Mean	1.69	3.03	0.71	2.20*	13.2
	SD	0.53	0.25	0.17	0.18	0.5
	n	10	10	10	10	10
32 PPM	Mean	0.59*	2.24*	0.23*	1.20*	9.4*
	SD	0.15	0.10	0.06	0.06	0.9
	n	10	10	10	10	10
260 PPM	Mean	0.10*	1.72*	0.06*	1.10*	2.5*
	SD	0.03	0.10	0.02	0.07	0.5
	n	9	9	10	10	10

Statistics: Anova + Dunnetts tests (two-sided): * P<0.05 (Exp.Unit = Animal)

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Table CC4-SUM
A Two-Generation Reproduction Study in Rats With DEF
Percent Cholinesterase Depression from Control
(Statistically Significant Activities Only)
Study Number 88-671-AK

Adults

	Premating		Termination		
Generation	PCHE	RCHE	PCHE	RCHE	BCHE
F0 Males	32 ppm (32%)	32 ppm (35%)	32 ppm (18%)	32 ppm (31%)	
	260 ppm (70%)	260 ppm (50%)	260 ppm (78%)	260 ppm (53%)	260 ppm (36%)
F1 Males		4 ppm (9%)			
		32 ppm (26%)		32 ppm (28%)	
	260 ppm (57%)	260 ppm (43%)	260 ppm (68%)	260 ppm (39%)	260 ppm (33%)
F0 Females			4 ppm (26%)	4 ppm (12%)	
	32 ppm (68%)	32 ppm (37%)	32 ppm (72%)	32 ppm (46%)	32 ppm (29%)
	260 ppm (91%)	260 ppm (49%)	260 ppm (90%)	260 ppm (52%)	260 ppm (81%)
F1 Females				4 ppm (7%)	
	32 ppm (59%)	32 ppm (28%)	32 ppm (72%)	32 ppm (49%)	32 ppm (29%)
	260 ppm (93%)	260 ppm (45%)	260 ppm (93%)	260 ppm (53%)	260 ppm (81%)

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Data Evaluation Report

009140

Compound Tribufos (DEF)

Citation
A Cross-Fostering study in rats using Tribufos (DEF®) administered in the diet, D.A. Eigenberg; Mobay, Corporate Toxicology Department, Study Number 88-971-BZ; Aug 29, 1991; MRID 420401-03

11/15/92

Reviewed by Robert P. Zendzian Ph.D.
Senior Pharmacologist
Health Effects Division

Core Classification Acceptable

Conclusion
Cross fostering study to determine if pup loss in study 88-671-AK was due to treatment of dams, pups in utero or both. Doses tested 0 and 260 ppm. Group II negative control-untreated pups & dams, Group I experimental-treated pups untreated dams, Group III experimental-untreated pups treated dams, Group IV positive control-treated pups treated dams. Mean pup loss 0.00, 0.47, 1.50 & 2.85 respectively. Cannibalism in treated dam groups (III & IV). Evidence for both mechanisms plus a synergistic effect in group IV.

Materials

Technical grade Tribufos
Straw colored liquid
Batch No; 85R-26-39
99.7% (9/88)
98.8% (3/89)
98.1% (9/89)
From Mobay Ag Chemicals Division

Male and female albino CD Sprague-Dawley rats, seven weeks old,
from Sasco Inc Omaha Nebraska

Experimental Design

Sixty males and 120 females were assigned randomly to each of four test groups of 15 males and 30 females each. Groups 1 and 2 received 0 ppm and groups 3 and 4 received 260 ppm tribufos in the diet. After 10 weeks on the test diet these animals were bred within their test groups. After birth pups from groups 1 and 3 were cross fostered so that the 0 ppm dams reared pups from 260 fed dams and the 260 ppm dams reared pups from 0 ppm dams. Pups from group 2 and 4 were cross fostered within the test groups. That is, pups from 0 ppm dams were raised by 0 ppm dams that were not their birth dams and the same with pups from 260 ppm dams.

Test material analysis

Test material was analyzed for identity, recovery in the feed, homogeneity in the feed, stability in the feed and concentration in the feed.

Breeding

After ten weeks on treated diet, 1 male and 2 females were cohabited for breeding for up to 21 days. Females were checked daily for vaginal plug and vaginal smears examined for sperm. When sperm was observed females were housed individually for gestation and lactation. At 21 days females not observed as breeding were caged individuallly for 24 days in case breeding had occured.

Parturition and cross-fostering

Beginning on day 21 of gestation, females were checked hourly (during working hours) for parturition. Upon completion of delivery pups were culled to four males and four females per litter. Pups were cross fostered as stated in the experimental design by transfering whole litters within approximately 36 hours of birth. Litters that were not cross-fostered and pups from groups II and IV were saved for a study to examine the fertility of F1 pups (study 89-971-DC).

Clinical observations

Rats were observed daily for morbidity, mortality and clinical signs in the cage. Animals were individually examined weekly.

Live and still born pups and sex distribution were determined for each litter. Litter counts and pup weights were obtained at birth (day 0) and on days 4, 7, 14 and 21.

Plasma, red blood cell and brain cholinesterase were determined on 10 females per dose group, plasma and RBC during week 8 and just prior to sacrifice and brain at termination.

Sacrifice

Culled pups were sacrificed by injection of euthanasia solution, adults and weanlings by CO_2 asphyxiation. Gross necropsy was not performed and no tissues were collected for histopathology.

Results

Analysis of dosed feed showed that test material was homeogeniously distributed and stable for 14 days at room temperature.

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Data collected during the study are summarized in Tables 2 through 7 from the report as follows;

Table 2, Pup observations summary.

Table 3, Average number of pups missing or cannibalized before cross foster.
Average number of pups missing or cannibalized after cross foster.

Table 4, Viability index.

Table 5, Affect (sic) of cannibalization on the 21-day viability index.

Table 6, Litter weight.

Table 7, Cholinesterase data.

The largest number of pup observations were found in control pups fostered by treated dams. Although the lest number of pup observations were reported in control pups fostered by control dams, they were only one or two less than treated pups by treated dams and treated pups by control dams.

Before cross foster, the mean number missing/cannibalized pups almost exclusively confined to liters from 260 ppm dams. After cross foster, mean missing/cannibalized were in the order Group IV (260 dams - 260 pups)> Group III (260 dams - control pups)> Group I (control dams - 260 pups)> Group II (control dams - control pups).

The viability index, for fostered pups, followed the same order as the missing/cannibalized after cross foster in that viability from lowest to highest followed the order Group IV, Group III, Group I, Group II. The effect of cannibalism on the day-21 viability index followed the same order.

Mean litter weights were similar on day 0 but growth was depressed in the order (least growth to most growth) Group IV, Group III, Group I, Group II.

Cholinesterase data showed a significant depression of activity in the dosed dams at week 9 and at termination, plasms and erythrocyte at both occasions and brain at termination.

Discussion

A 2-generation reproduction study of tirbufos in rats showed a significant pup loss at the high dose (260 ppm). Part of this loss was attributed to cannibalization of pups. Cannibalization may be either primary, in that dams kill and

eat normal pups or secondary in that dams kill and eat sick pups and/or eat dead pups. This study was designed to distinguish these two possibilities. Group II was the negative control in that untreated dams fostered pups from other untreated dams. Group IV was the positive control in that treated dams fostered pups from other treated dams. Group I was the experimental group for assesing the effect on pups of treated dams in that untreated dams fostered pups from treated dams. Group III was the experimental group for assesing the effect of treated dams in that treated dams fostered pups from untreated dams.

The origional study also showed an apparent decreased birth weight in the 260 ppm pups. This was considered as possibly due to the pups being weighed as long as 24 hours after birth. In this study the pups were weighed at birth directly before cross fostering.

Table A presents selected data on pup survival/loss and the cause of that loss. The least effect was in the negative control group were no pups were lost and the greatest effect was in the positive control grpup with a mean of 2.85 pups lost per litter. Losses also occured in both the treated pup group and the treated dam group, the greatest loss in the latter group. This indicates two effects, one in utero on the pups of treated dams and the second on the treated dam. A very crude attempt has been made to determine if these two effects together are additive or synergistic (greater than additive). The mean number of pups lost from Groups I and III are summed (this is permissable since the number of litters are essentially the same, 17 & 18). These sums are less than the group IV values, 84, 37 and 69 percent respectively, and indicate the possibility of a synergistic effect. Cannibalism can be considered due to treatment of the dams but the additional noncannibalistic loss was an effect on the pups secondary to treatment of the dams.

Litter weights were essentially the same at birth but a clear effect of dam treatment was observed at 21 days and was more than could be attributed to pup loss (Table 6).

Table A. Summary of selected pup data

	Mean number of pups Day 21			Viability Index				Viability Index Adjusted for cannibalization
	Missing	Cannibalized	Total	Day 4	Day 7	Day 14	Day 21	Day 21
Group II (24)a negative control Untreated Pups & Dams	0.00	0.00	0.00	100	100	100	100	100
Group I (17) Untreated Dams Treated pups	0.47	0.00	0.47	82	82	82	82	91
Group III (18) Treated dams Untreated Pups	1.17	0.33	1.50	81	68	63	63	83
Group IV (20) Positive Control Treated Dams Treated Pups	1.95	0.90	2.85	39	31	28	28	72
SUM Groups I & III	1.64	0.33	1.96					
(% of Group IV)	84	37	69					

a. number of litters

TABLE 2

MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT CROSS FOSTERING STUDY WITH DEF
STUDY NUMBER 88-971-BZ

PUP OBSERVATIONS SUMMARY

DAM #	FOSTER DAM #	PUP NUMBER	SEX	OBSERVATION	DAY(S) OBSERVED
CONTROL PUPS FOSTERED BY TREATED DAMS					
BZ0101	BZ3117	9	FEMALE	Bite mark and hematoma on chest.	7
BZ0102	BZ3123	3	MALE	Tip of tail missing.	21
BZ0109	BZ3128	10	FEMALE	Bite marks on dorsal side.	3
BZ0113	BZ3130	1	MALE	Cold and weak.	4
		2	MALE	Cold and weak.	4
		3	MALE	Cold and weak.	4
BZ0114	BZ3105	1	MALE	Weak.	4
		4	MALE	Weak.	4
		7	FEMALE	Weak.	4
		9	FEMALE	Weak.	4
		11	FEMALE	Weak.	4
BZ0117	BZ3116	2	MALE	Deep purple in color and cold.	4
		4	FEMALE	Deep purple in color and cold.	4
		5	FEMALE	Deep purple in color and cold.	4
		6	FEMALE	Deep purple in color and cold.	4
BZ0127	BZ3109	8	FEMALE	Tip of tail missing.	14-21
CONTROL PUPS FOSTERD BY CONTROL DAMS					
BZ0145	BZ0160	13	FEMALE	Enlarged right eye.	19-20
BZ0152	BZ0155	10	FEMALE	Hematoma covering whole head and neck.	0
TREATED PUPS FOSTERED BY CONTROL DAMS					
BZ3109	BZ0127	9	FEMALE	Unthrifty.	1
BZ3123	BZ0102	8	MALE	Moribund and sacrificed.	0-1
		9	MALE	Moribund and sacrificed.	0-1
BZ3130	NCF	1	MALE	Moribund and sacrificed.	0
TREATED PUPS FOSTERED BY TREATED DAMS					
BZ3132	BZ3140	3	MALE	Moribund and sacrificed.	3
BZ3151	BZ3133	6	FEMALE	Bite mark on ventral thorax.	10-13
BZ3143	BZ3145	12	FEMALE	Approximately one half of tail missing.	9-21

NCF = NOT CROSS FOSTERED.

TABLE 3

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MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT CROSS FOSTERING STUDY WITH TRIBUFOS
STUDY NUMBER 88-971-BZ

009140

AVERAGE NUMBER OF PUPS MISSING OR CANNIBALIZED PER LITTER AND NUMBER OF DAMS WITH LITTERS IN WHICH ONE OR BOTH OF THESE OCCURANCES WERE OBSERVED

BEFORE CROSS FOSTER (A)

		OBSERVATION		
		MISSING	CANNIBALIZED	TOTAL
AVG. PUPS/LITTER (B)				
	GROUP I N = 27	0.04	0.04	0.08
	GROUP II N = 24	0.00	0.00	0.00
	GROUP III N = 24	0.33	0.13	0.46
	GROUP IV N = 27	0.11	0.93	1.04
NUMBER OF DAMS (C)				
	GROUP I N = 27	1	1	2
	GROUP II N = 24	0	0	0
	GROUP III N = 24	1	3	4
	GROUP IV N = 27	3	8	11

(A) SOME INFORMATION WAS OBTAINED FROM ANIMALS THAT WERE NOT CROSS FOSTERED. THESE ANIMALS WERE OBSERVED UNTIL THE TIME THEY WERE NO LONGER AVAILABLE FOR CROSS FOSTER DUE TO TIME CONSTRAINTS. THEREFORE, INFORMATION FROM NON-CROSSED ANIMALS IS INCLUDED IN THE "BEFORE CROSS FOSTER" SUMMARY ONLY.

(B) GROUPS I AND II = CONTROL
GROUPS III AND IV = 260 PPM

(C) THIS IS THE NUMBER OF DAMS THAT HAD LITTERS IN WHICH PUPS WERE MISSING OR CANNIBALIZED.

AVG = AVERAGE
N = NUMBER OF LITTERS

000035

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TABLE 3

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MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT CROSS FOSTERING STUDY WITH TRIBUFOS
STUDY NUMBER 88-971-BZ

AVERAGE NUMBER OF PUPS MISSING OR CANNIBALIZED PER LITTER AND NUMBER OF DAMS WITH LITTERS IN WHICH ONE OR BOTH OF THESE OCCURANCES WERE OBSERVED

AFTER CROSS FOSTER

		OBSERVATION		
		MISSING	CANNIBALIZED	TOTAL
AVG. PUPS/LITTER (A)				
	GROUP I N = 17	0.47	0.00	0.47
	GROUP II N = 24	0.00	0.00	0.00
	GROUP III N = 18	1.17	0.33	1.50
	GROUP IV N = 20	1.95	0.90	2.85
NUMBER OF DAMS (B)				
	GROUP I N = 17	3	0	3
	GROUP II N = 24	0	0	0
	GROUP III N = 18	6	3	9
	GROUP IV N = 20	10	7	17

(A) THESE NUMBERS ARE ATTRIBUTABLE TO THE DAMS AND INDICATE HOW THEY DID AFTER CROSS FOSTERING TOOK PLACE.
- -GROUP I (CONTROL) DAMS HAD GROUP III (260 PPM) PUPS.
- -GROUP II (CONTROL) DAMS HAD GROUP II (CONTROL) PUPS.
- -GROUP III (260 PPM) DAMS HAD GROUP I (CONTROL) PUPS.
- -GROUP IV (260 PPM) DAMS HAD GROUP IV (260 PPM) PUPS.

(B) THIS IS THE NUMBER OF DAMS THAT HAD LITTERS IN WHICH PUPS WERE MISSING CANNIBALIZED.

AVG = AVERAGE

N = NUMBER OF LITTERS

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TABLE 4

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MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT CROSS FOSTERING STUDY WITH DEF
STUDY NUMBER 88-971-BZ
VIABILITY INDEX

*MEANS AND (STANDARD DEVIATIONS)**

LEVEL *	VIABILITY INDEX DAY 4	VIABILITY INDEX DAY 7	VIABILITY INDEX DAY 14	VIABILITY INDEX DAY 21
GROUP I (CONTROL)	82a (28)	82a (28)	82a (28)	82a (28)
GROUP II (CONTROL)	100b (0)	100b (0)	100b (0)	100b (0)
GROUP III (260 PPM)	81a (30)	68a (44)	63a (43)	63a (43)
GROUP IV (260 PPM)	39c (47)	31c (43)	28c (42)	28c (42)

* = VIABILITIES FOR DAYS 4, 7, 14 AND 21 WERE OBSERVED AFTER PUPS WERE GIVEN TO THEIR CROSS FOSTER DAM.

AFTER DAY 0:
GROUP I IS CONTROL DAMS WITH 260 PPM PUPS.
GROUP II IS CONTROL DAMS WITH CONTROL PUPS.
GROUP III IS 260 PPM DAMS WITH CONTROL PUPS.
GROUP IV IS 260 PPM DAMS WITH 260 PPM PUPS.

Values with the same letter are not statistically significantly different ($p \leq 0.05$).

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MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT

RAT CROSS FOSTERING STUDY WITH TRIBUFOS

STUDY NUMBER 88-971-BZ

AFFECT OF CANNIBALIZATION ON THE DAY-21 VIABILITY INDEX (%)

MEANS AND STANDARD DEVIATIONS

	Dose Level	Died Day 0 PC to Day 21	Cannibalized Day 0 PC to Day 21	% of Dead Cannibalized	Viability Index Day 21	Adjusted Day 21 Index*
	GROUP I					
N		17	17	17	17	17
MEAN		1.06	0.47	16.47	82.25	91.22b
SD		1.48	1.18	36.90	27.83	13.88
	GROUP II					
N		24	24	24	24	24
MEAN		0.00	0.00	0.00	100.00	100.00a
SD		0.00	0.00	0.00	0.00	0.00
	GROUP III					
N		18	18	18	18	18
MEAN		2.72	1.50	26.02	62.50	82.73b
SD		3.03	2.11	34.01	43.30	23.74
	GROUP IV					
N		21	21	21	21	21
MEAN		4.19	2.76	52.32	28.40	75.03b
SD		3.20	2.96	41.28	42.04	34.56

PC = Postcull
N = Number of litters
SD = Standard deviation

GROUP I = CONTROL DAMS WITH 260 PPM PUPS.
GROUP II = CONTROL DAMS WITH CONTROL PUPS.
GROUP III = 260 PPM DAMS WITH CONTROL PUPS.
GROUP IV = 260 PPM DAMS WITH 260 PPM PUPS.

* = Viability index day 21 - Cannibalization. This equation assumes that the only pups which died during the 21-day lactation were those which were not cannibalized or missing.

Values with the same letter are not statistically significantly different ($p \leq 0.05$).

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TABLE 6

MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT CROSS FOSTERING STUDY WITH TRIBUFOS
STUDY NUMBER 88-971-BZ
LITTER WEIGHT (GRAMS)

*MEANS AND (STANDARD DEVIATIONS)**

LEVEL	LITTER WEIGHT DAY 0 (A)	LITTER WEIGHT DAY 4	LITTER WEIGHT DAY 7	LITTER WEIGHT DAY 14	LITTER WEIGHT DAY 21
GROUP I (CONTROL)	6.5a (1)	10.4a (1)	15.2a (2)	30.6a (3)	50.6a (5)
GROUP II (CONTROL)	6.7a (0)	11.0a (1)	16.3a (1)	31.3a (2)	53.8a (4)
GROUP III (260 PPM)	6.8a (1)	7.5b (1)	11.1b (2)	21.0b (4)	34.9b (6)
GROUP IV (260 PPM)	6.6a (1)	7.5b (2)	9.6b (2)	21.0b (4)	34.9b (8)

(A) = DAY 0 LIVE WEIGHT.

*WEIGHTS FOR DAYS 4, 7, 14 AND 21 WERE OBSERVED AFTER PUPS WERE PLACED WITH THEIR CROSS FOSTER DAM.

AFTER DAY 0:
GROUP I = CONTROL DAMS WITH 260 PPM PUPS.
GROUP II = CONTROL DAMS WITH CONTROL PUPS.
GROUP III = 260 PPM DAMS WITH CONTROL PUPS.
GROUP IV = 260 PPM DAMS WITH 260 PPM PUPS.

Values with the same letter are not statistically significantly different ($p \leq 0.05$).

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TABLE 7

MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT CROSS FOSTERING STUDY WITH TRIBUFOS
STUDY NUMBER 88-971-BZ

009140

CHOLINESTERASE DATA (IU/ml)

MEANS AND STANDARD DEVIATIONS

9 WEEK BLEEDING

	DOSE GROUP	DOSE LEVEL	PLASMA CHOLINESTERASE	ERYTHROCYTE CHOLINESTERASE	BRAIN CHOLINESTERASE
	I	CONTROL			
NUMBER			10	10	.
MEAN			1.99	2.34	.
SD			0.40	0.19	.
	II	CONTROL			
NUMBER			10	10	.
MEAN			1.61	2.58	.
SD			0.39	0.18	.
	III	260 PPM			
NUMBER			10	10	.
MEAN			0.08*	1.04*	.
SD			0.03	0.05	.
	IV	260 PPM			
NUMBER			10	10	.
MEAN			0.12*	0.99*	.
SD			0.03	0.09	.
			TERMINAL BLEEDING		
	I	CONTROL			
N			10	10	10
MEAN			1.02	2.49	15.0
SD			0.15	0.14	0.90
	II	CONTROL			
N			10	10	10
MEAN			0.81	2.64	15.3
SD			0.13	0.26	1.80
	III	260 PPM			
N			10	10	10
MEAN			0.15*	1.18*	2.7*
SD			0.10	0.18	0.6
	IV	260 PPM			
N			10	10	10
MEAN			0.13*	1.13*	3.2*
SD			0.09	0.12	1.0

SD = Standard Deviation

*Statistically significantly different ($p \leq 0.05$) from the control group (groups I and II, and groups III and IV were combined for statistical comparison).

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TABLE 2

MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT CROSS FOSTERING STUDY WITH DEF
STUDY NUMBER 88-971-BZ

PUP OBSERVATIONS SUMMARY

DAM #	FOSTER DAM #	PUP NUMBER	SEX	OBSERVATION	DAY(S) OBSERVED
CONTROL PUPS FOSTERED BY TREATED DAMS					
BZ0101	BZ3117	9	FEMALE	Bite mark and hematoma on chest.	7
BZ0102	BZ3123	3	MALE	Tip of tail missing.	21
BZ0109	BZ3128	10	FEMALE	Bite marks on dorsal side.	3
BZ0113	BZ3130	1	MALE	Cold and weak.	4
		2	MALE	Cold and weak.	4
		3	MALE	Cold and weak.	4
BZ0114	BZ3105	1	MALE	Weak.	4
		4	MALE	Weak.	4
		7	FEMALE	Weak.	4
		9	FEMALE	Weak.	4
		11	FEMALE	Weak.	4
BZ0117	BZ3116	2	MALE	Deep purple in color and cold.	4
		4	FEMALE	Deep purple in color and cold.	4
		5	FEMALE	Deep purple in color and cold.	4
		6	FEMALE	Deep purple in color and cold.	4
BZ0127	BZ3109	8	FEMALE	Tip of tail missing.	14-21
CONTROL PUPS FOSTERD BY CONTROL DAMS					
BZ0145	BZ0160	13	FEMALE	Enlarged right eye.	19-20
BZ0152	BZ0155	10	FEMALE	Hematoma covering whole head and neck.	0
TREATED PUPS FOSTERED BY CONTROL DAMS					
BZ3109	BZ0127	9	FEMALE	Unthrifty.	1
BZ3123	BZ0102	8	MALE	Moribund and sacrificed.	0-1
		9	MALE	Moribund and sacrificed.	0-1
BZ3130	NCF	1	MALE	Moribund and sacrificed.	0
TREATED PUPS FOSTERED BY TREATED DAMS					
BZ3132	BZ3140	3	MALE	Moribund and sacrificed.	3
BZ3151	BZ3133	6	FEMALE	Bite mark on ventral thorax.	10-13
BZ3143	BZ3145	12	FEMALE	Approximately one half of tail missing.	9-21

NCF = NOT CROSS FOSTERED.

TABLE 3

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MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT CROSS FOSTERING STUDY WITH TRIBUFOS
STUDY NUMBER 88-971-BZ

009140

AVERAGE NUMBER OF PUPS MISSING OR CANNIBALIZED PER LITTER AND NUMBER OF DAMS WITH LITTERS IN WHICH ONE OR BOTH OF THESE OCCURANCES WERE OBSERVED

BEFORE CROSS FOSTER (A)

		OBSERVATION		
		MISSING	CANNIBALIZED	TOTAL
AVG. PUPS/LITTER (B)				
	GROUP I N = 27	0.04	0.04	0.08
	GROUP II N = 24	0.00	0.00	0.00
	GROUP III N = 24	0.33	0.13	0.46
	GROUP IV N = 27	0.11	0.93	1.04
NUMBER OF DAMS (C)				
	GROUP I N = 27	1	1	2
	GROUP II N = 24	0	0	0
	GROUP III N = 24	1	3	4
	GROUP IV N = 27	3	8	11

(A) SOME INFORMATION WAS OBTAINED FROM ANIMALS THAT WERE NOT CROSS FOSTERED. THESE ANIMALS WERE OBSERVED UNTIL THE TIME THEY WERE NO LONGER AVAILABLE FOR CROSS FOSTER DUE TO TIME CONSTRAINTS. THEREFORE, INFORMATION FROM NON-CROSSED ANIMALS IS INCLUDED IN THE "BEFORE CROSS FOSTER" SUMMARY ONLY.

(B) GROUPS I AND II = CONTROL
GROUPS III AND IV = 260 PPM

(C) THIS IS THE NUMBER OF DAMS THAT HAD LITTERS IN WHICH PUPS WERE MISSING OR CANNIBALIZED.

AVG = AVERAGE
N = NUMBER OF LITTERS

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TABLE 3

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MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT CROSS FOSTERING STUDY WITH TRIBUFOS
STUDY NUMBER 88-971-BZ

AVERAGE NUMBER OF PUPS MISSING OR CANNIBALIZED PER LITTER AND NUMBER OF DAMS WITH LITTERS IN WHICH ONE OR BOTH OF THESE OCCURANCES WERE OBSERVED

AFTER CROSS FOSTER

		OBSERVATION		
		MISSING	CANNIBALIZED	TOTAL
AVG. PUPS/LITTER (A)				
	GROUP I N = 17	0.47	0.00	0.47
	GROUP II N = 24	0.00	0.00	0.00
	GROUP III N = 18	1.17	0.33	1.50
	GROUP IV N = 20	1.95	0.90	2.85
NUMBER OF DAMS (B)				
	GROUP I N = 17	3	0	3
	GROUP II N = 24	0	0	0
	GROUP III N = 18	6	3	9
	GROUP IV N = 20	10	7	17

(A) THESE NUMBERS ARE ATTRIBUTABLE TO THE DAMS AND INDICATE HOW THEY DID AFTER CROSS FOSTERING TOOK PLACE.
-GROUP I (CONTROL) DAMS HAD GROUP III (260 PPM) PUPS.
-GROUP II (CONTROL) DAMS HAD GROUP II (CONTROL) PUPS.
-GROUP III (260 PPM) DAMS HAD GROUP I (CONTROL) PUPS.
-GROUP IV (260 PPM) DAMS HAD GROUP IV (260 PPM) PUPS.

(B) THIS IS THE NUMBER OF DAMS THAT HAD LITTERS IN WHICH PUPS WERE MISSING/ CANNIBALIZED.

AVG = AVERAGE

N = NUMBER OF LITTERS

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TABLE 4

MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT CROSS FOSTERING STUDY WITH DEF
STUDY NUMBER 88-971-BZ
VIABILITY INDEX

*MEANS AND (STANDARD DEVIATIONS)**

LEVEL *	VIABILITY INDEX DAY 4	VIABILITY INDEX DAY 7	VIABILITY INDEX DAY 14	VIABILITY INDEX DAY 21
GROUP I (CONTROL)	82a (28)	82a (28)	82a (28)	82a (28)
GROUP II (CONTROL)	100b (0)	100b (0)	100b (0)	100b (0)
GROUP III (260 PPM)	81a (30)	68a (44)	63a (43)	63a (43)
GROUP IV (260 PPM)	39c (47)	31c (43)	28c (42)	28c (42)

* = VIABILITIES FOR DAYS 4, 7, 14 AND 21 WERE OBSERVED AFTER PUPS WERE GIVEN TO THEIR CROSS FOSTER DAM.

AFTER DAY 0:
GROUP I IS CONTROL DAMS WITH 260 PPM PUPS.
GROUP II IS CONTROL DAMS WITH CONTROL PUPS.
GROUP III IS 260 PPM DAMS WITH CONTROL PUPS.
GROUP IV IS 260 PPM DAMS WITH 260 PPM PUPS.

Values with the same letter are not statistically significantly different ($p \leq 0.05$).

TABLE 5

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MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT

RAT CROSS FOSTERING STUDY WITH TRIBUFOS

STUDY NUMBER 88-971-BZ

AFFECT OF CANNIBALIZATION ON THE DAY-21 VIABILITY INDEX (%)

MEANS AND STANDARD DEVIATIONS

	Dose Level	Died Day 0 PC to Day 21	Cannibalized Day 0 PC to Day 21	% of Dead Cannibalized	Viability Index Day 21	Adjusted Day 21 Index*
	GROUP I					
N		17	17	17	17	17
MEAN		1.06	0.47	16.47	82.25	91.22b
SD		1.48	1.18	36.90	27.83	13.88
	GROUP II					
N		24	24	24	24	24
MEAN		0.00	0.00	0.00	100.00	100.00a
SD		0.00	0.00	0.00	0.00	0.00
	GROUP III					
N		18	18	18	18	18
MEAN		2.72	1.50	26.02	62.50	82.73b
SD		3.03	2.11	34.01	43.30	23.74
	GROUP IV					
N		21	21	21	21	21
MEAN		4.19	2.76	52.32	28.40	75.03b
SD		3.20	2.96	41.28	42.04	34.56

PC = Postcull
N = Number of litters
SD = Standard deviation

GROUP I = CONTROL DAMS WITH 260 PPM PUPS.
GROUP II = CONTROL DAMS WITH CONTROL PUPS.
GROUP III = 260 PPM DAMS WITH CONTROL PUPS.
GROUP IV = 260 PPM DAMS WITH 260 PPM PUPS.

* = Viability index day 21 – Cannibalization. This equation assumes that the only pups which died during the 21-day lactation were those which were not cannibalized or missing.

Values with the same letter are not statistically significantly different ($p \leq 0.05$).

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TABLE 6

MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT CROSS FOSTERING STUDY WITH TRIBUFOS
STUDY NUMBER 88-971-BZ
LITTER WEIGHT (GRAMS)

*MEANS AND (STANDARD DEVIATIONS)**

LEVEL	LITTER WEIGHT DAY 0 (A)	LITTER WEIGHT DAY 4	LITTER WEIGHT DAY 7	LITTER WEIGHT DAY 14	LITTER WEIGHT DAY 21
GROUP I (CONTROL)	6.5a (1)	10.4a (1)	15.2a (2)	30.6a (3)	50.6a (5)
GROUP II (CONTROL)	6.7a (0)	11.0a (1)	16.3a (1)	31.3a (2)	53.8a (4)
GROUP III (260 PPM)	6.8a (1)	7.5b (1)	11.1b (2)	21.0b (4)	34.9b (6)
GROUP IV (260 PPM)	6.6a (1)	7.5b (2)	9.6b (2)	21.0b (4)	34.9b (8)

(A) = DAY 0 LIVE WEIGHT.

*WEIGHTS FOR DAYS 4, 7, 14 AND 21 WERE OBSERVED AFTER PUPS WERE PLACED WITH THEIR CROSS FOSTER DAM.

AFTER DAY 0:
GROUP I = CONTROL DAMS WITH 260 PPM PUPS.
GROUP II = CONTROL DAMS WITH CONTROL PUPS.
GROUP III = 260 PPM DAMS WITH CONTROL PUPS.
GROUP IV = 260 PPM DAMS WITH 260 PPM PUPS.

Values with the same letter are not statistically significantly different ($p \leq 0.05$).

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TABLE 7

MOBAY CORPORATION - CORPORATE TOXICOLOGY DEPARTMENT
RAT CROSS FOSTERING STUDY WITH TRIBUFOS
STUDY NUMBER 88-971-BZ

009140

CHOLINESTERASE DATA (IU/ml)

MEANS AND STANDARD DEVIATIONS

9 WEEK BLEEDING

	DOSE GROUP	DOSE LEVEL	PLASMA CHOLINESTERASE	ERYTHROCYTE CHOLINESTERASE	BRAIN CHOLINESTERASE
	I	CONTROL			
NUMBER			10	10	.
MEAN			1.99	2.34	.
SD			0.40	0.19	.
	II	CONTROL			
NUMBER			10	10	.
MEAN			1.61	2.58	.
SD			0.39	0.18	.
	III	260 PPM			
NUMBER			10	10	.
MEAN			0.08*	1.04*	.
SD			0.03	0.05	.
	IV	260 PPM			
NUMBER			10	10	.
MEAN			0.12*	0.99*	.
SD			0.03	0.09	.
			TERMINAL BLEEDING		
	I	CONTROL			
N			10	10	10
MEAN			1.02	2.49	15.0
SD			0.15	0.14	0.90
	II	CONTROL			
N			10	10	10
MEAN			0.81	2.64	15.3
SD			0.13	0.26	1.80
	III	260 PPM			
N			10	10	10
MEAN			0.15*	1.18*	2.7*
SD			0.10	0.18	0.6
	IV	260 PPM			
N			10	10	10
MEAN			0.13*	1.13*	3.2*
SD			0.09	0.12	1.0

SD = Standard Deviation

*Statistically significantly different ($p \leq 0.05$) from the control group (groups I and II, and groups III and IV were combined for statistical comparison).

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Data Evaluation Report 009140

Compound Tribufos (DEF)

Citation
A dietary reproductive toxicity study investigation the fertility of F1 rats using Tribufos (DEF®), D.A. Eigenberg; Mobay, Corporate Toxicology Department, Study Number 88-971-DC; Aug 27, 1991; MRID 420401-02

Reviewed by Robert P. Zendzian Ph.D. 11/6/95
Senior Pharmacologist
Health Effects Division

Core Classification Unacceptable

Conclusion
The following footnotes were contained in the report;
"Due to an error, the control and 260 ppm rats received a mixture of control and 260 ppm feed for one day during week 13 of the study (i.e., mating/gestation phase).
"Due to a feeding error, terminal cholinesterase values were obtained from 6 high dose and 8 control animals."
No explanation was found in the test. It is not certain how the feeding errors, particularly the second might have affected the study.

Materials

Technical grade Tribufos
Straw colored liquid
Batch No; 85R-26-39
98.7% (3/28/89)
98.1% (9/12/89)
From Mobay Ag Chemicals Division

Male and female albino CD Sprague-Dawley rats, pups from Mobay study 88-971-BZ; Aug 29, 1991

Experimental Design

Male and female pups from Mobay study 88-971-DC were utilized for this study. Pups were from Group II - pups from untreated dams cross fostered with untreated dams and from Group IV - pups from treated dams cross fostered with treated dams. Pups were treated with 0 or 260 ppm tribufos in the diet respectively from weaning. After 10 weeks on the test diet these F1 animals were bred within their test groups (30 per sex per test group).[a]

Test material analysis

Test material was analyzed for concentration in the feed.

a. "Due to an error, the control and 260 ppm rats received a mixture of control and 260 ppm feed for one day during week 13 of the study (i.e., mating/gestation phase)."

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Breeding

One male and one female were cohabited for breeding for up to 21 days. Females were checked daily for vaginal plug and vaginal smears examined for sperm. When sperm was observed females were housed individually for gestation and lactation. Unmated females were cohabited with a second proven male for up to 7 days. Whether or not breeding was observed these females were subsiquently housed individually for gestation and lactation.

Clinical observations

Rats were observed daily for morbidity, mortality and clinical signs in the cage. Animals were individually examined weekly.

Plasma, red blood cell and brain cholinesterase were determined on 10 adults per sex per group, plasma and RBC during week 8 and just prior to sacrifice and brain at termination. Due to a feeding error, terminal cholinesterase values were obtained from 6 high dose and 8 control females.

Sacrifice

Females were sacrificed on day 20 of gestation and males after completion of breeding. All females were necropsied to determine if pregnant (implantation sites or pups present).

Results

Test material concentrations in the nominal dose of 260 ppm were 240 ppm week 1 and 237 ppm week 14.

No clinical signs indicative of cholinesterase toxicity were observed.

Fertility indices are presented in Table 2 from the report. Value were 93% control and 83% 260 ppm. The differences were not statistically significant.

Cholinesterase activity is presented in Table 3 from the report. All values are significantly depressed at 260 ppm.

The following footnotes were found in the report. Since there was no further explanation, it is impossible to determine what affect they may have had on the study. This may have been of critical importance since only 8 control and 6 high dose females were available for cholinesterase analysis out of 30 females for each dose.

"Due to an error, the control and 260 ppm rats received a mixture of control and 260 ppm feed for one day during week 13 of the study (i.e., mating/gestation phase).

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"Due to a feeding error, terminal cholinesterase values were obtained from 6 high dose and 8 control animals."

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TABLE 2

Fertility Indices of F0 Dams
in a Rat Reproduction Study Using Technical Tribufos

Study Number 89-971-DC

Dose Group	Number Co-housed	Number Sperm Positive	Number with Implantation Sites or Pups Present	Fertility Index %
Control	30	30	28	93
260.0 ppm	30	30	25	83

$$\text{Fertility Index (\%)} = \frac{\text{\# of pregnant females (a)}}{\text{\# of sperm positive females (b)}} \times 100$$

(a) = Any female with pups and/or implantation sites present in uterus at time of necropsy.

(b) = Includes females with pups and/or implantation sites, that were not sperm positive.

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MOBAY Toxicology Department
Study : 89-971-DC
Species : Rat
Generation : F0

TABLE 3
Premating Cholinesterase Activity in a Rat Reproduction Study Using Technical Tribufos

---

G R O U P M E A N S

M A L E S		DAY 51 PChe IU/ml	DAY 51 RChe IU/ml
CONTROL	Mean	0.50	2.76
	SD	0.08	0.19
	n	10	10
HIGH	Mean	0.16*	1.32*
	SD	0.03	0.08
	n	10	10

---

*Statistically significantly different from the control group ($p \leq 0.05$).

MOBAY Toxicology Department
Study : 89-971-DC
Species : Rat
Generation : F0

TABLE 3
Premating Cholinesterase Activity in a Rat Reproduction Study Using Technical Tribufos

G R O U P M E A N S			
F E M A L E S		Day 51 PChe IU/ml	Day 51 RChe IU/ml
CONTROL	Mean	1.68	2.64
	SD	0.42	0.16
	n	10	10
HIGH	Mean	0.13*	1.35*
	SD	0.04	0.08
	n	10	10

*Statistically significantly different from the control group ($p \leq 0.05$).

MOBAY Toxicology Department
Study : 89-971-DC
Species : Rat
Generation : F0

TABLE 3
Terminal Cholinesterase Activity in a Rat Reproduction Study Using Technical Tribufos

G R O U P M E A N S

M A L E S		Day 86 PChe IU/ml	Day 86 RChe IU/ml	Day 86 BChe IU/g
CONTROL	Mean	0.53	2.62	15.5
	SD	0.11	0.32	2.0
	n	10	10	10
HIGH	Mean	0.12*	1.25*	10.8*
	SD	0.05	0.10	0.8
	n	10	10	10

*Statistically significantly different from the control group ($p \leq 0.05$).

MOBAY Toxicology Department
Study : 89-971-DC
Species : Rat
Generation : F0

TABLE 3
Terminal Cholinesterase Activity in a Rat Reproduction Study Using Technical Tribufos

G R O U P M E A N S

F E M A L E S		Day 85 PChe IU/ml	Day 85 RChe IU/ml	Day 85 BChe IU/g
CONTROL	Mean	2.00	2.44	15.1
	SD	0.37	0.20	1.3
	n	8	8	8
HIGH	Mean	0.13*	1.03*	4.7*
	SD	0.02	0.11	1.8
	n	6	6	6

*Statistically significantly different from the control group ($p \leq 0.05$).

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033443

Chemical:	**S,S,S-Tributyl phosphorotrithioate**
PC Code:	**074801**
HED File Code	**13000 Tox Reviews**
Memo Date:	**02/11/92**
File ID:	**TX009140**
Accession Number:	**412-02-0280**

HED Records Reference Center
04/10/2002